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<p>(21) International Application Number: PCT/US94/02184</p> <p>(22) International Filing Date: 23 February 1994 (23.02.94)</p> <p>(30) Priority Data: 08/021,030 23 February 1993 (23.02.93) US</p> <p>(71) Applicant: PHARMAKON USA, INC. [US/US]; One State Street Plaza, New York, NY 10004 (US).</p> <p>(71)(72) Applicant and Inventor: NEIRON, Johel, M. [AU/AU]; 9 Alder Sea Road, Perth, W.A. (AU).</p> <p>(74) Agents: KALOW, David, A. et al.; Lieberman & Nowak, 292 Madison Avenue, New York, NY 10017 (US).</p>		<p>(81) Designated States: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAP patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p>
<p>(54) Title: THERAPEUTIC HERBAL COMPOSITION</p> <p>(57) Abstract</p> <p>A therapeutic herbal composition including <i>Trigonella foenum-graecum</i> seed, <i>Syzygium aromaticum</i> fruit, <i>Allium sativum</i> bulb, <i>Cinnamomum zeylanicum</i> bark, <i>Saussurea costus</i> root and <i>Euphorbia lathyris</i> bud have been shown effective in reducing cholesterol, and triglycerides. This herbal composition has use in lowering cholesterol and treating arthritis, blood pressure and Alzheimer's disease. It is also effective as a bitters tonic.</p>		

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Therapeutic Herbal Composition

Background of the Invention

The subject invention relates generally to a
5 therapeutic herbal composition, and in particular to a
herbal composition which includes *Trigonella foenum-graecum*
seed, *Syzygium aromaticum* fruit, *Allium sativum* bulb,
Cinnamomum zeylanicum bark, *Saussurea costus* root and
Euphorbia lathyris bud. This therapeutic herbal composition
10 is formed from a synergistic combination of herbs which are
useful in lowering cholesterol, and treating arthritis,
blood pressure and Alzheimer's disease. It is also useful
as a bitters tonic, and has been approved as a bitters tonic
by the Australian Therapeutic Goods Administration.

15 Although the use of various herbs has been described in
related areas, the synergistic combination of the subject
invention has never previously been described.

Japanese Patent Publication No. 4,005,237 teaches the
combination of *Cinnamomum sieboldii* and *Allium sativum* for
20 superoxide scavenging in the treatment of inflammatory
disorders. German Patent Publication No. 3,724,341 teaches
the use of *Cinnamomum zeylanicum* as an anti-inflammatory
agent which exerts a synergistic anti-inflammatory effect in
combination with *Punica granatum* cortex, *Cardamon*
25 *zingiberaceae* fruit and *Piper longum* fruit.

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In view of the above, there exists a great need for therapeutic compositions useful in lowering cholesterol, and treating arthritis, blood pressure and Alzheimer's disease. Although not wishing to be bound by theory, it is believed that the composition of herbs described herein functions to produce a synergistic interaction, and thus represents a potential tool in the treatment of high cholesterol, arthritis, high blood pressure and Alzheimer's disease, as well as a general bitters tonic.

10 Summary of the Invention

The subject invention provides a therapeutic composition which comprises *Trigonella foenum-graecum* seed, *Syzygium aromaticum* fruit, *Allilum sativum* bulb, *Cinnamomum zylanicum* bark, *Saussurea costus* root, and *Euphorbia lathyris* bud in amounts effective to produce a physiological benefit.

Detailed Description of the Invention

The subject invention will now be described in terms of its preferred embodiments. These embodiments are set forth to aid in the understanding of the subject invention, but are not to be construed as limiting.

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The subject composition is that described below:

		<u>wt.</u>	<u>% of wt.</u>	<u>% wt. range</u>
	<i>Trigonella foenum-graecum</i> seed	305 mg	52.5	5 - 95
5	<i>Syzygium aromaticum</i> fruit	55 mg	9.5	1 - 50
	<i>Allilum sativum</i> bulb	55 mg	9.5	1 - 50
	<i>Cinnamomum zylanicum</i> bark	55 mg	9.5	1 - 50
	<i>Saussurea costus</i> root	55 mg	9.5	1 - 50
10	<i>Euphorbia lathyris</i> bud	<u>55 mg</u> 580 mg	9.5	1 - 50

The composition supplies the physiologically important chemicals listed below:

	Choline	Calcium
	Phosphorous	Iron
15	Magnesium	Sodium
	Potassium	Zinc
	Vitamin A	Thiamine HCl
	Riboflavin	Nicotinic Acid
	Ascorbic Acid	Lecithin
20	Phytosterols	Tryptophane
	Beta Carotene	Colchicine

The biological active components include choline and inositol.

The above herbs are typically dried and ground to a fine powder. All weights are expressed in milligrams and all percentages are by weight of the essential elements in the composition. The composition is typically an intimate mixture of powders. However, extracted herbs may also be used.

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The known biological active components include choline and thiamine. Under normal conditions a 580 mg dose would be administered several times daily. The dosage of course may vary depending on body weight and other conditions readily determinable by those skilled in the art who have read the subject application. Administration is typically oral, with administration being via a capsule. In addition to the above herbs, various fillers, such as ash, may be present.

10 The following study was done to evaluate the efficacy of the subject composition. Four hundred people, in groups of one hundred people each, took part in the study as follows:

15 100 people on a weight loss and lower lipid diet and taking the subject composition.

 100 people on a weight loss and lower lipid diet and taking a placebo.

 100 people without the diet and taking the subject composition.

20 100 people without diet and taking a placebo.

All subjects were referred to by general practitioners, and details of medical status, including previous illnesses, medication and blood pressure, were kept.

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The following evaluations were performed:

- * Check on weight
- * Interview with dietitian monitoring daily dietary intake
- * Checks on lipids and liver enzymes
- 5 * Determination of likelihood of compliance

The purpose of the study was to determine whether the subject composition taken in capsule form 680 mg each (580 mg of the composition), twice daily for 18 weeks, lowers:

10 Total Cholesterol
 Triglycerides
 APO A1 B2
 RATIO
 Increase HDL

15 From the above trial, 200 subjects receiving a placebo (a combination of soya bean flower and sugar) showed no significant changes at the end of 10 weeks and treatment was discontinued.

20 From the 100 subjects treated with diet and the subject composition, eight discontinued treatment after six weeks, fifteen discontinued after fifteen weeks and one died. Based on fifteen weeks of treatment with diet, it was noted that there was a decreased in cholesterol and triglycerides by average of 22%.

25 Of the 100 subjects taking the subject composition together with diet, 76 subjects reported constitutional weight loss averaging 9 kg.

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- 5 Total cholesterol decrease by 58%
 Triglyceride decreased by 61%
 LDL/VLDL decrease by 29%
 Ratio decrease by up to 75%
 HDL increase by average of 80%

Of the 100 subjects taking the subject composition without diet, six subjects discontinued treatment due to strong body odor and balance of 94 subjects reported constitutionally:

- 10 51 subjects - Cholesterol reduced by 8-15%
 Triglyceride reduced by 30-42%
 LDL/VLDL reduced by 6-19%
 Ratio Reduced by 14-33%
 HDL increased by 62%
- 15 43 subjects - Cholesterol reduced by 3-11%
 Triglyceride reduced by 15-30%
 LDL/VLDL reduced by 1-7%
 Ratio Reduced by 9-20%
 HDL increased by 22%
- 20 Dosage 12 capsules per day for the first 6 weeks.
 for study: Thereafter reduced to 8 capsules per day
 (equivalent to 1 capsule per 6.7 kg of body weight).

- 25 Empirical evidence from laboratory tests attests to the
good efficacy of capsules containing the subject composition during its two years shelf life. The main bioactive ingredients include choline, thiamine HCl, ascorbic acid, nicotinic acid, lecithin and phytosterols, which are reported by the British Pharmacopoeia to be effective
- 30 against coronary atherosclerosis and lowering high cholesterol and triglyceride levels. The hygroscopicity to moisture content varies during storage and distribution from 6.8% to 10% while maintaining normal function.

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The biodecomposition in digestibility test within 0.2% pepsin solution complies with analysis of Association of Analytical Chemists for 28% digestive residue at temperature 42°-45°C during 16 hours supporting good quality herbal ingredients. Clinical research shows that ratios of HDL (High Density Lipoproteins) to LDL (Low Density Lipoproteins) lies in their respective functions for reduced blood cholesterol levels.

Normally the powder is encapsulated in moisture permeable gelatine doses of zero size and next is stored in 350 mls polyvinyl chloride bottles at range temperature 20-30°C. This prevents powder texture, white color and a bioactivity from changing as a result of variations in night and day temperatures, as well as keeping smell and taste unimpaired during storage. Moreover, the cholesterol lowering action of the subject composition is stabilized by radiation sterilization or using ethylene oxide penetration at elevated temperature, i.e. about 70°C.

The stability data do not contain detectable concentration of degradation substances and periodical bacteriological tests under a high humidity environment proved satisfactory.

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Upon reading the subject application, various
embodiments will become obvious to those skilled in the art.
These embodiments are to be considered within the scope and
spirit of the subject invention, which is only to be limited
5 by the claims which follow and their equivalents.

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What is claimed is:

1. A therapeutic composition which comprises *Trigonella foenum-graecum* seed, *Syzygium aromaticum* fruit, *Allilum sativum* bulb, *Cinnamonmum zyelanicum* bark, *Saussurea costus* root, and *Euphorbia lathyris* bud in amounts effective to produce a physiological benefit.
2. A composition of claim 1, wherein the *Trigonella foenum-graecum* seed is present in an amount of from about 5 to about 95 weight percent of the composition, *Syzygium aromaticum* fruit is present in an amount of from about 1 to about 50 weight percent of the composition, *Allilum sativum* bulb is present in an amount from about 1 to about 50 weight percent of the composition, *Cinnamonmum zyelanicum* bark is present in an amount from about 1 to about 50 weight percent of the composition, *Saussurea costus* root is present in an amount from about 1 to about 50 weight percent of the composition, and *Euphorbia lathyris* bud is present in an amount from about 1 to about 50 weight percent of the composition.
3. A composition of claim 2, wherein the *Trigonella foenum-graecum* seed is present in an amount of about 52.5% by weight of the composition, *Syzygium aromaticum* fruit is present in an amount of about 9.5% by weight of the composition, *Allilum sativum* bulb is present in an amount of about 9.5% by weight of the composition, *Cinnamonmum*

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zyelanicum bark is present in an amount of about 9.5% by weight of the composition, *Saussurea costus* root is present in an amount of about 9.5% by weight of the composition, and *Euphorbia lathyris* bud is present in an amount of about 9.5% by weight of the composition.

4. A composition of claim 1 further comprising a filler.

5. A capsule comprising the composition of claim 1.

6. A capsule of claim 5, wherein the *Trigonella foenum-graecum* seed is present in an amount of about 52.5% by weight of the composition, *Syzygium aromaticum* fruit is present in an amount of about 9.5% by weight of the composition, *Allilum sativum* bulb is present in an amount of about 9.5% by weight of the composition, *Cinnamomum* *zyelanicum* bark is present in an amount of about 9.5% by weight of the composition, *Saussurea costus* root is present in an amount of about 9.5% by weight of the composition, and *Euphorbia lathyris* bud is present in an amount of about 9.5% by weight of the composition.

7. A capsule of claim 6, wherein the *Trigonella foenum-graecum* seed is present in an amount of about 305 mg, *Syzygium aromaticum* fruit is present in an amount of about 55 mg, *Allilum sativum* bulb is present in an amount of about

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5 mg, *Cinnamomum zeylanicum* bark is present in an amount of about 55 mg, *Saussurea costus* root is present in an amount of about 55 mg, and *Euphorbia lathyris* bud is present in an amount of about 55 mg.

INTERNATIONAL SEARCH REPORT

 International application No.
 PCT/US94/02184

A. CLASSIFICATION OF SUBJECT MATTER

IPC(S) : A61K 35/78, 9/48

US CL : 424/195.1, 451

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/195.1, 451; 514/824, 825

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 5,073,545 (ARIMA ET AL.) 17 December 1991, see entire document.	1-7
A	US, A, 4,933,177, (GROLIER ET AL.) 12 June 1990, see the entire document.	1-7
A	US, A, 4,569,839 (GROLIER ET AL.) 11 February 1986, see the entire document.	1-7
A	US, A, 4,767,618 (GROLIER ET AL.) 30 August 1988, see the entire document.	1-7
A	US, A, 5,176,913 (HONERLAGEN ET AL.) 05 January 1993, see the entire document.	1-7

☐ Further documents are listed in the continuation of Box C.

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